Rachel Clough

Dr. Kim Eagle: Hello, my name is Kim Eagle. I am the Hewlett Professor of Internal Medicine and one of the directors of the Frankel Cardiovascular Center at the University of Michigan. I also have the pleasure of being the study chair for a very interesting registry called GenTAC. It studies genetically triggered aortic conditions; we have a number of sites in the United States.

Today, I am interviewing Dr. Rachel Clough. Rachel is at the National Institute for Health Research and she's a clinical lecturer in the Division of Imaging Sciences at Kings College in London. Her work in the area of dynamic imaging is fascinating.

Welcome, Rachel.

Dr. Rachel Clough: (nods) Hi, Kim; thanks for having me.

Dr. Eagle: I've been following your career since I first saw some of the interesting work you presented several years ago.

Dr. Clough: Ok.

Dr. Eagle: And, it seems to me like you're on the verge of moving the field of imaging, because we're moving from kind of static aortic size, and kind of shape, to things that are potentially far more important. That is flow patterns and so forth. Tell our audience today a little bit about your work and where you think it's taking us.

Dr. Clough: Thanks, Kim. So, it's very kind of you to say that I'm moving things forwards. I spenttwo or three years out of clinica practice three years ago focusing on developing dynamic imaging techniques using MRs specifically for aortic disease. And like you said as a group we think that moving forwards from more static techniques like CT, typically, to dynamic techniques, particularly using MR, will be more useful in the future. And so what we've done so far is develop methods to be able to try to understand the underlying hemodynamics and biomechanics in patients with aortic disease, studying, for example, like I said, flow patterns, as well as other flow derived parameters, say wall sheer stress and velocities and so on. And so in specifically related to your question about flow patterns, so we studies specifically patients with aortic dissection and we have evaluated the flow patterns in the false lumen and shown that patients that have highly helical flow, so high rates of rotation in their flow, are more prone to form aneurysms.

Dr. Eagle: Ok. So this makes sense because if the flow is laminar then you presume that the amount of energy the heart has imparted with the jet is following the line of the aorta but if it's helical then presumably that's increasing the wall stress on an already damaged aorta – is that right?

Dr. Clough: Yea, so there are various groups who have tried to study what these flow patterns mean in relation to aneurysm formation, not just in the aorta but in, for example, the cerebral circulation as well as related to carotid disease. And, there are various theories and I'm not sure if it's actually a unified theory about exactly what the direct mechanism is but people assume that there are changes in wall sheer stress which have an effect on the endothelial function and extracellular matrix remodeling. But exactly what amount of wall sheer stress you need and

what type of wall sheer stress parameters you should be measuring is, I think, still to be decided.

Dr. Eagle: What are some of the barriers that are holding the technology back from being available in day to day practice?

Dr. Clough: So nitially it was about, I suppose, just developing the actual, for example, MR sequences that you need to be able to do this but they're now freely available and many centers can use these type of methods. You need a bit of local expertise in terms of how to apply the sequence, how to reconstruct and analyze the data, but again if you have interested people that's not beyond many people. I think one of the problems would be standardizing the techniques across different centers. There's typically a view in the MR community that between different vendors, even if, between the different vendors there are some variation in the type of data you get, so somehow standardizing that as well as the way you analyze the data would be quite important so really get a good idea of the predictive value of these parameters.

Dr. Eagle: When I think, Rachel, about current imaging techniques, a lot of our techniques have a set protocol maybe for every disorder in echo or CT. And you mention the sequence. And MR is complicated, isn't it? You have to design the sequencing to fit your question and that's not necessarily standardized.

Dr. Clough: So you're right about standardizing the imaging techniques. The one thing that I would just say before we talk on about standardizing the MR protocols, there's already some lack of standardization, I think, between some of the CT protocols we use, particularly for aortic dissections, so as you know false lumen thrombosis is one of the current clinical end points or imaging end points we use to re-stratify patients. But actually if you look at the methods that people use to try to determine false lumen thrombosis, they're not really either clearly described in the literature or they just vary between different institutions. And what we found is that when we study false lumen thrombosis, we assume that there's no contrast in the false lumen and there must be thrombose there. But actually it may be that the contrast hasn't got there by the time that you acquire the imaging data.

Dr. Eagle: I see.

Dr. Clough: So even with what we consider to be current clinical reference tools, there's in some respect, no standardization between the way that those scans are being done. And then to answer your question more directly about the MR protocols, you're right there is many different bits and pieces you can change on the sequences and change on the acquisition protocols but probably there aren't so many of those parameters directly related to the clinical interpretation of that data and those features could be standardized between different centers.

Dr. Eagle: I see. So you almost need a clinician and a physicist…

Dr. Clough: Yeah…

Dr. Eagle: To define the sequencing for a given patient.

Dr. Clough: Yup.

Dr. Eagle: And then you need software that allows you to rapidly analyze what the data looks like and put it into a clinical framework.

Dr. Clough: Yeah, so what we've developed in our center is we have an aortic imaging list and at the minute, it's mainly me that goes just because I have a particular interest in it and quite quickly developed a standardized way of evaluating the data and then we produced a clinical report with pretty much the same parameters described in that report, with images which accompany that still images, just snap shots, to explain some of what we're trying to describe in the written report.

Dr. Eagle: So in your center currently, are you measuring, for instance, helicity which you've talked about and is that part of the clinical management now at Kings College?

Dr. Clough: So, we do mention helicity in the reports but we tend to provide a much more clear overview of what's actually happening in that patient's aorta. So we start by describing aortic size and dimensions, which you typically would, and then using some of the dynamic anatomy sequences, we talk about the amounts of flat mobility and at which part of the cardiac cycle that happens. And then we talk about the amount of flow, the velocity of flow and the flow patterns that all builds up a kind of comprehensive picture of what's happening in that patient.

Dr. Eagle: Wonderful. So yeah, I mean really think your work and several other people that I've seen, is setting the stage for much more personalized follow-up that we've just focused on size of the true lumen and false lumen and maybe morphology of segments compared to one another but this technology potentially allows us to personalize care. We might even use it to follow patients and say is this aortic healing itself or is it acting like it's being more injured over time. Is that right?

Dr. Clough: Yeah I think you're right. So there have been a number of CT based studies which have tried to identify parameters which identify high risk people but you know, like we said, size, position of entry tear, number of entry tears, number of false lumens, and so on. And probably all of those indirectly measuring the underlying hemodynamics and biomechanics. And then if we looked at the literature to the two large trials, ADSORB and INSTEAD, we see that even in people who followed the trial recommended protocol individuals within those groups which have crossed over or had poor outcomes and that's, as you said, I think related to patients who are quite different and by putting them into like one or two groups doesn't necessarily begin to give us a clear picture of exactly what these patients are like. So hopefully using these methods, these MR methods, we'll be able to understand individual patients much better in the future.

Dr. Eagle: Part of the excitement of the whole field is that as genetics moves forward and then potentially proteomics, where we measure blood proteins that are reacting to whatever is happening in the aorta and then we fit that with more granular imaging, we have the potential to really change kind of from a shotgun approach to a real laser guided approach to each patient.

Dr. Clough: Yeah, I think that's really exciting and that slightly, that feeds back into your initial question about the relationship of wall sheer stress and helicity and what does it actually mean. So people think it changes gene expression but actually when we have these new methods, you're describing, that we also actually understand it is gene expression which is changing some other feature.

Dr. Eagle: Rachel, do you foresee a day where we could use biological tags. So you use imaging acquisition but potentially antibodies or other tags that would further elucidate basic biological functions in these kinds of patients?

Dr. Clough: For sure. Soin Kings College London we already have a molecular imaging group who use targeted MR contrast agents to look at various aspects of vessel walls, so collagen, elastin, fibrin, and so on. As far as I know, they've mainly done it in animal models so far, but I presume as the technology develops, that will be integrated into human and clinical work as well.

Dr. Eagle: Excellent. Well, on behalf of our viewing audience, I want to thank you for taking time today to talk about your very exciting work.

Dr. Clough: Thanks, Kim; thanks for having me.